KNIPE et al.

Serial No.: Page 2 of 17 08/278,601

#### Amendments to the Claims

This listing of claims will replace all prior versions, and listing, of claims in the application.

### Listing of Claims:

### 1-11. Cancelled

12 (Previously presented). A method of eliciting an immune response in a mammal comprising administering to the mammal an effective amount of a mutated herpesvirus in a pharmaceutically acceptable carrier, the herpesvirus having a mutation in one or more genes encoding a protein essential for viral genome replication to render the herpesvirus replication defective, said mutant herpesvirus having an ability to effect an antibody subclass shift of IgG2a/IgG upon *in vivo* administration to said mammal.

13 (Original). The m ethod of claim 12 wherein the herpesvirus is selected from the group consisting HSV-1, HSV-2, VZV, EBV, CMV, HHV-6 or HHV-7.

14 (Original). The method of claim 13 wherein the herpesvirus is HSV-1 or HSV-2.

15 (Original). The method of claim 14 wherein the mutation is in the gene or genes encoding the proteins ICP8 or ICP 27.

# 16 (Cancelled).

17 (Currently amended). A method of treating a mammal for <u>herpetic encephalitis</u>, <u>the method</u> comprising administering to the mammal an effective amount of a mutated herpesvirus in a pharmaceutically acceptable carrier, the herpesvirus having a mutation in one or more genes encoding a protein essential for viral genome replication to render the herpesvirus

KNIPE et al.

Serial No.:

08/278,601

Page 3 of 17

replication defective, said mutant herpesvirus having an ability to effect an antibody subclass shift of IgG2a/IgG upon *in vivo* administration to said mammal.

18 (Previously presented). A method of eliciting an immune response treating herpetic stromal keratitis in a mammal, the method comprising administering to the mammal an effective amount of a mutated herpesvirus in a pharmaceutically acceptable carrier, the herpesvirus having a mutation in one or more genes encoding a protein essential for viral genome replication to render the herpesvirus replication defective, said mutant herpesvirus having an ability to effect an antibody subclass shift of IgG2a/IgG upon *in vivo* administration to said mammal.

19 (Original). The method of claim 18 wherein the herpesvirus is selected from the group consisting of HSV-1, HSV-2, VZV, EBV, CMV, HHV-6 or HHV-7.

20 (Original). The method of claim 19 wherein the herpesvirus is HSV-1 or HSV-2.

21 (Original). The method of claim 20 wherein the mutation is in the gene or genes encoding the proteins ICP8 or ICP 27.

22-30. Cancelled

31 (Previously presented). A composition in a pharmaceutically accepted carrier comprising:

a mutated herpesvirus characterized by a mutation in at least one gene encoding a protein essential for viral genome replication of said herpesvirus, thereby,

rendering the virus genome replication defective; and,

the herpesvirus comprising one or more heterologous genes; wherein,

the mutated herpesvirus is capable of infecting a mammalian cell and of eliciting an immune response to heterologous gene products in a mammal treated with the herpesvirus.

Applicant: Serial No.: KNIPE et al. 08/278,601

Page 4 of 17

32-35. Cancelled

36 (Previously presented). A composition comprising a mutated herpesvirus capable of infecting a mammalian cell;

said herpesvirus comprising a mutation in one or more early genes encoding a protein essential for viral genome replication to render the herpesvirus replication defective; and,

said herpesvirus comprising one or more heterologous genes encoding heterologous gene products; wherein,

the mutated herpesvirus is capable of infecting a mammalian cell and of eliciting an immune response to the heterologous gene products in a mammal treated with said herpesvirus.

37-40. Cancelled

41 (Previously presented). A method of inducing an immune response against herpesvirus in a mammal comprising administering to said mammal a vaccine comprising a mutated herpesvirus in a pharmaceutically accepted carrier, said herpesvirus having a mutation in one or more genes encoding a protein essential for viral genome replication to render the herpesvirus replication defective and further encoding one or more heterologous genes.

42-49. Cancelled

50 (Cancelled).

51 (Currently amended). The immunogenic composition of claim 53 50, wherein the herpesvirus is selected from the group consisting of HSV-1, HSV-2, VZV, EBV, HHV-6 and HHV-7.

Applicant: Serial No.: KNIPE et al. 08/278,601

Page 5 of 17

52 (Currently amended). The immunogenic composition of claim 51, wherein the herpesvirus is HSV-1 or HSV-2.

immunogenic composition comprising a pharmaceutically acceptable carrier and a mutated herpesvirus capable of infecting a mammalian cell and of eliciting an immune response in a mammal immunized with the composition, wherein the herpesvirus includes two or more deletion mutations in one or more genes encoding HSV-1, ICP27; or HSV-1, ICP8; or in a corresponding early gene in a non-HSV-1 herpesvirus, and the mutation renders the herpesvirus incapable of replication, wherein the gene encoding ICP27 comprises a first nonsense mutation and the gene encoding ICP8 comprises a second deletion mutation, wherein either mutation or the combination of the mutations renders the herpesvirus incapable of replication.

54 (Cancelled).

55 (Cancelled).

56 (Cancelled).

57 (Currently amended). A method of eliciting an immune response in a mammal, the method comprising administering to the mammal an immunogenic composition comprising a mutated herpesvirus capable of infecting a mammalian cell and eliciting an immune response, wherein the herpesvirus includes two or more mutations in one or more genes encoding HSV-1, ICP27; or HSV-1, ICP8; or in a corresponding early gene in a non-HSV-1 herpesvirus, and the mutations render the herpesvirus incapable of replication, wherein one mutation is a nonsense mutation and another mutation is a deletion mutation.

58 (Previously presented). The method of claim 57, wherein said herpesvirus is selected from the group consisting of HSV-1, HSV-2, VZV, EBV, HHV-6 and HHV-7.

KNIPE et al.

Serial No.:

08/278,601

Page 6 of 17

59 (Previously presented). The method of claim 57, wherein said herpesvirus is HSV-1 or HSV-2.

60 (Currently amended). The method of claim 57, wherein the gene encoding ICP27 comprises a first nonsense mutation and the gene encoding ICP8 comprises a second deletion mutation, wherein either mutation or the combination of the mutations renders the herpesvirus incapable of replication.

- 61 (Cancelled).
- 62 (Cancelled).
- 63 (Currently amended). A method of treating a mammal to elicit an immunogenic response, the method comprising administering to the mammal an effective amount of an immunogenic composition comprising a mutated herpesvirus in a pharmaceutically acceptable carrier, wherein the herpesvirus includes two or more <u>deletion</u> mutations in one or more genes encoding HSV-1, ICP27; or HSV-1, ICP8; or in a corresponding early gene in a non-HSV-1 herpesvirus, thereby, the mutations render the herpesvirus incapable of replication, and the mutant herpesvirus induces an immunogenic effect upon *in vivo* administration to the mammal.

### 64. Cancelled.

65 (Previously presented). The immunogenic composition of claim 50, wherein one mutation is a deletion mutation and the other mutation is a nonsense mutation.

### 66. Cancelled.

KNIPE et al.

Serial No.:

08/278,601

Page 7 of 17

67 (Previously presented). The method according to claim 63, wherein the herpesvirus contains a mutation in at least two of the genes, wherein one mutation is a deletion mutation and the other mutation is a nonsense mutation.

68 (Previously presented). An immunogenic composition comprising a pharmaceutically acceptable carrier and a replication defective herpesvirus which expresses a heterologous protein, wherein said herpesvirus is characterized by a mutation in at least one gene encoding HSV-1, ICP27; or HSV-1, ICP8; or in a corresponding early gene in a non-HSV-1 herpesvirus, and the mutation renders the herpesvirus incapable of replication.

69 (Previously presented). The immunogenic composition of claim 68, wherein the herpesvirus is HSV-1, HSV-2, VZV, EBV, HHV-6 or HHV-7.

# 70. Cancelled.

71 (Previously presented). The immunogenic composition of claim 68 wherein the gene is HSV-1 ICP-27.

72 (Previously presented). The immunogenic composition of claim 68 wherein said gene is HSV-1 or HSV-2 ICP-8.

73 (Previously presented). The immunogenic composition of claim 68, wherein said herpesvirus is characterized by a mutation in two or more genes encoding HSV-1, ICP27; or HSV-1, ICP8; or in a corresponding early gene in a non-HSV-1 herpesvirus, and the mutation renders the herpesvirus incapable of replication.

# 74. Cancelled.

KNIPE et al.

Serial No.:

08/278,601

Page 8 of 17

75 (Previously presented). The immunogenic composition of claim 73, wherein said genes encode ICP8 and ICP 27.

76 (Previously presented). The immunogenic composition of claim 68, wherein the gene encoding ICP27 comprises a first mutation and the gene encoding ICP8 comprises a second mutation, thereby, the herpesvirus expressing the heterologous protein is rendered incapable of replication.

77 (Previously presented). The immunogenic composition of claim 73, wherein the gene encoding ICP27 comprises a first mutation, thereby, the herpesvirus expressing the heterologous protein is rendered incapable of replication.

78 (Previously presented). The immunogenic composition of claim 73, wherein the gene encoding ICP8 comprises a first mutation, thereby, the herpesvirus expressing the heterologous protein is rendered incapable of replication.

79 (Previously presented). The immunogenic composition of claim 73, wherein the herpesvirus expressing the heterologous protein is HSV-1 or HSV-2.

- 80 (Previously presented). The immunogenic composition of claim 79, wherein the heterologous protein is an immunogenic protein from a virus, bacteria, fungi or parasite.
- 81 (Previously presented). The immunogenic composition of claim 80, wherein the immunogenic protein is from an RNA or DNA virus.
- 82 (Previously presented). The immunogenic composition of claim 81, wherein the immunogenic protein is from a Human Immunodeficiency Virus (HIV).
- 83 (Previously presented). The immunogenic composition of claim 82, wherein the immunogenic protein elicits a B- and/or T-cell immune response.

KNIPE et al.

Serial No.:

08/278.601

Page 9 of 17

84 (Previously presented). A method of eliciting an immune response in a mammal, the method comprising administering to the mammal an immunogenic composition comprising a mutated herpesvirus, expressing a heterologous protein and is capable of infecting a mammalian cell and eliciting an immune response, wherein the herpesvirus includes a mutation in a gene encoding HSV-1, ICP27; or HSV-1, ICP8; or in a corresponding early gene in a non-HSV-1 herpesvirus, and the mutated herpesvirus is rendered incapable of replication.

- 85 (Previously presented). The method of claim 84, wherein the herpesvirus expressing the heterologous protein is selected from the group consisting of HSV-1, HSV-2, VZV, EBV, HHV-6 and HHV-7.
- 86 (Previously presented). The method of claim 84, wherein the herpesvirus expressing the heterologous protein is HSV-1 or HSV-2.
- 87 (Previously presented). The method of claim 84, wherein the gene encoding ICP27 comprises a first mutation and the gene encoding ICP8 comprises a second mutation, thereby, the herpesvirus expressing the heterologous protein is rendered incapable of replication.
- 88 (Previously presented). The immunogenic composition of claim 84, wherein the heterologous protein is an immunogenic protein from a virus, bacteria, fungi or parasite.
- 89 (Previously presented). The immunogenic composition of claim 84, further comprising a mutation in at least two of the genes.
- 90 (Previously presented). The immunogenic composition of claim 84, further comprising a mutation in at least two of the genes, wherein one mutation is a deletion mutation and the other mutation is a nonsense mutation.

KNIPE et al.

Serial No.:

08/278,601

Page 10 of 17

91 (Previously presented). A method of treating a mammal to elicit an immunogenic

response, the method comprising administering to the mammal an effective amount of an

immunogenic composition comprising a mutated herpesvirus expressing a heterologous protein

in a pharmaceutically acceptable carrier, wherein the herpesvirus includes a mutation in a gene

encoding HSV-1, ICP27; or HSV-1, ICP8; or in a corresponding early gene in a non-HSV-1

herpesvirus, thereby, the mutated herpesvirus is rendered incapable of replication, and the mutant

herpesvirus induces an immunogenic effect upon in vivo administration to the mammal.

92 (Previously presented). The method according to claim 91, wherein the herpesvirus

contains a mutation in at least two of the genes and expresses a heterologous protein.

93 (Previously presented). The method according to claim 91, wherein the herpesvirus

contains a mutation in at least two of the genes, wherein one mutation is a deletion mutation and

the other mutation is a nonsense mutation.

94 (Previously presented). The method according to claim 91, wherein the herpesvirus

contains at least two mutations in the genes.

95 (Previously presented). The method according to claim 94, wherein one mutation is

a deletion mutation and the other mutation is a nonsense mutation.

96 (Previously presented). The method of claim 91, wherein the heterologous protein

is an immunogenic protein from a virus, bacteria, fungi or parasite.

97 (Previously presented). The method according to claim 91, wherein the in vivo

immunogenic effect in a mammal comprises a B- cell and/or T cell response.

98 (Cancelled).

KNIPE et al.

Serial No.:

08/278,601

Page 11 of 17

99 (Currently amended). The immunogenic composition of claim 104 98, wherein the herpesvirus is selected from the group consisting of HSV-1, HSV-2, VZV, EBV, HHV-6 and

HHV-7.

100 (Currently amended). The immunogenic composition of claim 104 98, wherein

the herpesvirus is HSV-1 or HSV-2.

101 (Previously presented). The immunogenic composition of claim 99, wherein a gene

encoding ICP27 comprises a nonsense mutation and a gene encoding ICP8 comprises a deletion

mutation.

102 (Cancelled).

103 (Cancelled).

104 (Previously presented). The immunogenic composition of claim 98 An

immunogenic composition comprising a pharmaceutically acceptable carrier and a mutated

herpesvirus capable of infecting a mammalian cell and of eliciting an immune response in a

mammal immunized with the composition, wherein the herpesvirus includes two or more

mutations in one or more genes encoding a protein essential for viral genome replication to

render the herpesvirus incapable of replication, wherein one mutation is a nonsense mutation and

another mutation is a deletion mutation.

Please add the following new claims, which are exactly the same as original claims 12 -

15, allowed prior to declaration of interference.

105 (New). A method of treating an immunomodulatory disease in mammel in need

thereof comprising administering to the mammal an effective amount of a mutated herpesvirus in

a pharmaceutically acceptable carrier, the herpesvirus having a mutation in one or more genes

encoding a protein essential for viral genome replication to render the herpesvirus replication

KNIPE et al.

Serial No.:

08/278,601

Page 12 of 17

defective, said mutant herpesvirus having an ability to effect an antibody subclass shift of IgG2a/IgG upon *in vivo* administration to said mammal.

106 (New). The method of claim 105 wherein the herpesvirus is selected from the group consisting HSV-1, HSV-2, VZV, EBV, CMV, HHV-6 or HHV-7.

107 (New). The method of claim 106 wherein the herpesvirus is HSV-1 or HSV-2.

108 (New). The method of claim 107 wherein the mutation is in the gene or genes encoding the proteins ICP8 or ICP 27.